

CURRICULUM VITAE : Georges Wagnières

PERSONAL INFORMATION

NAME:	Wagnières	FIRST NAME:	Georges
DATE OF BIRTH:	2 nd May, 1962	NATIONALITY:	Swiss
MARITAL STATUS:	Married	CHILDREN	Three (8, 5 and 3 years)
PERMANENT HOME ADDRESS:	Chemin de Plantaz 56 CH-1095 Lutry Switzerland	CURRENT WORK ADDRESS:	LPAS Bâtiment de Chimie Swiss Federal Institute of Technology (EPFL) CH-1015 Lausanne Switzerland
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EDUCATION

Master in Management of Technology (January 2001 - December 2001)

Ecole des Hautes Etudes Commerciales (HEC) of the Lausanne's University / Swiss Federal Institute of Technology (EPFL): (Program comprising 550 hours of courses given in english in Lausanne, plus 60 hours given at the Business school of the University of Texas, Austin, USA. Moreover, this program involves an internship of 4 months).

Postdoctoral training (Research Fellow) (July 1993 - August 1994)

Harvard Medical School, Wellman Laboratories of Photomedicine, Boston, MA, USA.

Study: Characterization of photosensitizers and endogenous fluorophores in biological tissues by optical spectroscopy.

Doctorat ès Science (PhD) (May 1987 - April 1992)

Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland; Department of Physics;

Thesis topics: Photochemotherapy and photodetection of cancers using phototoxic and fluorescing agents.

Diplôme de physique (MS) (September 1981 - May 1986)

Lausanne University, Lausanne, Switzerland; Department of Physics.

Diploma topics: Radio Frequency Size Effect in Aluminium: Measurement of the Electrons Scattering Frequency.

Diplôme de culture générale scientifique (June 1979 - June 1981)

Gymnase Cantonal de la Cité, Lausanne, Switzerland.

PROFESSIONAL EXPERIENCE

From September 1994 to present

Appointed 'Adjoint scientifique' (Project Leader) at the Swiss Federal Institute of Technology in Lausanne (EPFL), Switzerland. A position with research, teaching and management responsibilities.

- **Management activities:**
 - Responsible for the scientific and financial planning, as well as for the management of the "Cancer photodetection and photodynamic therapy (PDT)" group of the EPFL (14 coworkers).
 - Responsible for the obtaining of subsidies.
 - Creation and management of industrial and academic partnerships (about twenty institutions).
 - Responsible of the electronics and mechanics workshops of the laboratory (two technicians).
- **Teaching activities:**
 - Invited Professor at the University of Paris XIII, "Laboratoire de Physique des Lasers" (1998).
 - Supervision of 6 Ph.D. students.
 - Responsible of the diploma, basic and advanced physics laboratories performed in the PDT group (5 students/year).
- **Research Topics and technical skills.**
 - Preclinical and clinical evaluation of photosensitizers for photodynamic therapy.
 - Development of light distributors for endoscopic photodynamic therapy.
 - Study of the light dosimetry and of the tissue optical properties.
 - Clinical detection of early cancers by fluorescence imaging during endoscopy.
 - In vivo measurement of the vascular and tissular oxygen concentration using phosphorescing molecular probes.
 - Clinical tissue spectrofluorometry (steady-state and time-resolved) applied to: 1) the study of the pharmacokinetics of photosensitizers, 2) the spectral design of cancer photodetection apparatus.
 - Study of the histological and cellular localization of drugs by fluorescence microscopy.

From July 1993 to August 1994

Appointed Postdoctoral fellow at the **Harvard Medical School**, Wellman Laboratories of Photomedicine, Boston, MA, USA.

Research Topics and technical skills.

- Development of a microspectrofluorometer to measure quantitatively the fluorescence of endogenous and/or exogenous fluorochromes in histological sections.
- Study of a new approach to characterize biological tissues based on the use of environmentally sensitive fluorochromes.
- Preclinical study of the fluence rate effect and the photobleaching of photosensitizers.

Creation of collaborations.

- Prof. J. Fujimoto, Department of Electrical Engineering and Computer Sciences, Massachusetts Institute of Technology (MIT), Boston, MA, USA.
Determination of the staging of superficial cancers by optical coherence tomography (OCT).
- Prof. B. Wilson and Prof. M. Patterson, Hamilton Regional Cancer Center, Ontario, Canada.
Study of environmentally sensitive fluorochromes by frequency-domain time-resolved spectrofluorometry.

Teaching activity.

- Courses and seminars given in the tutorials program of the Wellman Laboratories. Subject: "Tissue characterization by fluorescence spectroscopy"

From May 1992 to June 1993

Same activity as between September 1994 and today (see above).

From May 1987 to April 1992

PhD student at the Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland.

Research: Photochemotherapy and photodetection of cancers using phototoxic and fluorescing agents.

A C H I E V E M E N T S

ORIGINAL SCIENTIFIC REALIZATIONS:

- Development of instrumentations for the endoscopic detection of early superficial cancers and for their treatment by photodynamic therapy.
- Development of an original instrumentation to obtain fluorescence/phosphorescence lifetime images in real time and endoscopically in the frequency domain.
- Proposition of a novel method for the *in vivo* tissue characterization and cancer detection based on the use of fluorochromes sensitive to the physico-chemical properties of their environment. This principle is the basis technology of a start-up company (spin off of the Harvard Medical School).
- Development of a novel method to measure the tissue optical properties based on the use of the "CW spatial Fourier-transform reflectometry" approach.
- Application of optical coherence tomography (OCT) for the assessment of the staging of superficial carcinoma.
- Development of an experimental method to measure the fluorescence quantum yield of fluorophores in biological tissues.

CREATIONS:

- Co-founder and President of a spin-off biotech company (PhotoDerma SA; 1 coworker), founded in Mai 2003, which develops a technology for permanent hair removal.
- Co-founder and President of a spin-off biotech company (Medlight SA; 5 coworkers), founded in July 1997, which develops, produces and commercializes light distributors for photodynamic therapy.
- Significant contribution to the creation and financing of a multidisciplinary research group (Lausanne's PDT group) involving 15 coworkers active in the field of biomedical optics.

TRANSFER OF TECHNOLOGY:

- Most of our results and instrumental developments performed in the field of cancer detection by fluorescence imaging and photodynamic therapy have been transferred to medical instrumentation industries.
- The results of our studies regarding the optimization and assessment of new photosensitizers for photodynamic therapy have been transferred to several pharma companies.

INVENTIONS:

- Inventor of 10 patents (see the annex). Most of these patents are accepted at an international level. Three more patents are pending.

FINANCIAL SUPPORTS FOR ACADEMIC RESEARCH:

- More than 4'600'000 US\$ obtained since 1993.
 - (60% from Swiss scientific research programs and Institutions; 15% from European Programs; 20% from Industries; 5% from Foundations).
 - (25% as unique applicant; 55% as co-applicant responsible for the scientific management; 20% as co-applicant).

L A N G U A G E S

FRENCH: Fluently written and spoken (mother language)

ENGLISH: Fluently written and spoken

GERMAN: Working knowledge

C O M P U T E R S K I L L S

Familiar with Apple and PC systems and office applications (Word, Endnote, Excel, Powerpoint, Acrobat, KaleidaGraph, Photoshop, NIH Image, Canvas, Eudora, Internet explorer, Netscape).

D I S T I N C T I O N S

- Invited Professor at the University of Paris XIII (1998).
- Grant for advanced researcher provided by the Swiss national funds for scientific research; financial support for one year at the Harvard Medical School, Boston USA (1993 - 1994).
- Student award of the international photodynamic association, Buffalo, NY. (July 1990).

S O C I E T I E S

- The International Society for Optical Engineering
- Optical Society of America
- American Society for Photobiology
- European Optical Society
- Biomedical Optics Society
- American Society for Laser Medicine and Surgery
- The International Photodynamic Association
- Association Vaudoise des Chercheurs en Physique
- Société Suisse de Physique

B O A R D S

- Topics Editor of "The Journal of Biomedical Optics".
- Chair of the Conference "Diagnostic Optical Spectroscopy", European Conference on Biomedical Optics, Munich, Germany; June 2003.
- President of the scientific committee and chairman of the "Troisième Colloque National OPT-DIAG '2000: "Optique pour le diagnostic Medical", Paris, France; May 2000.
- Chairman and member of the scientific committee of numerous international conferences.
- Evaluation of numerous grant requests addressed to financial sources (Pôles de Recherche Français, Fonds pour la recherche scientifique Belge, Netherlands Organisation for Scientific Research, Katholieke Universiteit Leuven).
- Referee for: Applied Physics B; Lasers in Medical Science; Optics Letters; Applied Optics; Photochemistry Photobiology; Gastroenterology; Progress in Biomedical Optics.
- Member of the scientific committee and chairman of numerous international conferences.
- Member of five foreign Ph.D. examining boards.

E X T R A - C U R R I C U L A R A C T I V I T I E S

I enjoy outdoor activities namely skiing, jogging, volley-ball, sailing and mountain walking. Moreover, I appreciate family leisure. I have an interest for gastronomy and like to discover new cultures through traveling.

R E F E R E N C E S U P O N R E Q U E S T

ANNEX

P U B L I C A T I O N S

Publications "Peer reviewed".

- 76) S. Andrejevic-Blant, A. Major, F. Lüdicke, J.-P. Ballini, G. Wagnières, H. van den Bergh and M.-F. Pelte, "Time-dependent hexyl-Aminolevulinic acid induced PPIX histopathologic distribution after topical application in patients with cervical intraepithelial neoplasia: A fluorescence microscopy study", submitted.
- 75) P. Wyss, R. Caduff, Y. Tadir, A. Degen, G. Wagnières, V. Schwarz, U. Haller, M. Fehr, "Photodynamic endometrial ablation: Morphological study", *Lasers in Surgery and Medicine*, 32(4), pp 305-309, 2003.
- 74) A. Degen, T. Gabrecht, L. Mosimann, M. Fehr, R. Hornung, V. Schwarz, Y. Tadir, R. Steiner, P. Wyss, "Photodynamic endometrial ablation for the treatment of dysfunctional uterine bleeding: A preliminary report", in press in: *Am. J. Obstetrics & Gynecology*.
- 73) A. Degen, T. Gabrecht, M. Fehr, G. Wagnières, R. Caduff, B. Imthurn, P. Wyss, "Influence of the menstrual cycle on the ALA induced protoporphyrin IX fluorescence in the endometrium: a clinical study", submitted.
- 72) Th. Stepinac, S. Chamot, E. Rungger, P. Ferrez, J.-L. Munoz, H. van den Bergh, C. Pournaraz, Ch. Riva, G. Wagnières, "Real-Time Monitoring of PDT-induced Retinal Vascular Damage by Phosphorescence Lifetime Imaging of a Pd-Porphyrin Oxygen Probe Used as Photosensitizer", submitted.
- 71) F. Lüdicke, T. Gabrecht, N. Lange, G. Wagnières, H. van den Bergh, L. Berclaz and A. Major, "Photodynamic diagnosis of ovarian cancer using aminolevulinic acid hexylester: A preclinical study", *Brit. J. of Cancer*, 88(11), pp 1780-1784, 2003.
- 70) F. Borle, A. Radu, G. Wagnières, H. van den Bergh, Ph. Monnier, "Evaluation of the photosensitizer Tookad for photodynamic therapy on the Syrian golden hamster cheek pouch model: Light dose, drug dose and drug-light interval effects", in press in: *Photochem. Photobiol.*
- 69) F. Borle, A. Radu, G. Wagnières, H. van den Bergh, Ph. Monnier "Evaluation of the photosensitizer Tookad on the Syrian golden hamster cheek pouch model: Response of photodynamic therapy on chemically induced squamous cell carcinoma versus healthy mucosae", in press in: *Brit. J. Cancer*.
- 68) S. Andrejevic Blant, Th. Glanzmann, J.-P. Ballini, G. Wagnières, H. van den Bergh, Ph. Monnier, "Uptake and localization of mTHPC (Foscan®) and its 14C-labeled form in normal and tumor tissues of hamster squamous cell carcinoma model: a comparative study", *British Journal of Cancer*, 87(12), pp 1470-1478, 2002.
- 67) A. Marti, P. Jichlinski, N. Lange, J.-P. Ballini, L. Guillou, F. Bosman, G. Wagnières, H. van den Bergh, P. Kucera, H.-J. Leisinger, "In vivo photosensitization of transitional cell carcinoma of the bladder with aminolevulinic acid or hexylester of aminolevulinic acid induced protoporphyrin IX", submitted.
- 66) A. Radu, R. Conde, G. Wagnières, Ch. Fontolliet, H. van den Bergh, Ph. Monnier, "Mucosal ablation with photodynamic therapy in the esophagus: Optimization of Light Dosimetry in the sheep model", in press in: *Gastrointestinal Endoscopy*.
- 65) R. Conde, Th. Glanzmann, A. Radu, J.-P. Ballini, H. van den Bergh, Ch. Fontolliet, Ph. Monnier and G. Wagnières, "Assessment of the sheep as a model to optimize photodynamic therapy with Foscan® in the esophagus", submitted.
- 64) M. Zellweger, D. Goujon, A. Radu, P. Grosjean, Th. Stepinac, H. van den Bergh, Ph. Monnier and G. Wagnières, "Detection of early bronchial cancer by autofluorescence: first clinical results with an improved system", submitted.
- 63) Th. Stepinac, Ch. Felley, P. Jornod, N. Lange, G. Wagnières, Ch. Fontolliet, H. van den Bergh, Ph. Monnier, P. Michetti, G. Dorta, "Endoscopic Fluorescence Detection of Dysplasia and Early Adenocarcinoma in Barrett's Esophagus after Administration of 5-Aminolevulinic Acid: a controlled Clinical Trial", *Endoscopy*, 35(8), pp 663-668, 2003.
- 62) D Goujon, M Zellweger, A Radu, P Grosjean, B-C Weber, H van den Bergh, Ph monnier, G. Wagnières. In vivo autofluorescence imaging of early cancers in the human tracheo-bronchial tree with a spectrally optimized system. *J Biomed Opt*, 8(1), pp 17-25, 2003.
- 61) Th. Stepinac, P. Grosjean, A. Woodtli, P. Monnier, H. van den Bergh, G. Wagnières, "Optimization of the Diameter of a Radial Irradiation Device for Photodynamic Therapy in the Esophagus", *Endoscopy*, 34(5), pp 411-415, 2002.
- 60) C. Wilder-Smith, P. Wilder-Smith, P. Grosjean, H. van den Bergh, A. Woodtli, Ph. Monnier, G. Dorta, F. Meister, G. Wagnières, "Photoeradication of Helicobacter pylori using 5-aminolevulinic acid: preliminary human studies", *Laser in Surgery and Medicine*, 31(1), pp 18-22, 2002.
- 59) G. Wagnières, A. Mcwilliams and S. Lam, "Lung cancer Imaging by autofluorescence bronchoscopy", in: *Handbook of Biomedical Fluorescence*, M.-A. Mycek and B. Pogue Editors, Marcel Dekker Inc., pp 361-396, 2002.

58) S. Andrejevic Blant, P. Grosjean, J.-P. Ballini, G. Wagnières, H. van den Bergh, Ch. Fontolliet and Ph. Monnier, "Localisation of tetra(m-hydroxyphenyl)chlorin (Foscan®) in human healthy tissues and squamous cell carcinomas of the upper aero-digestive tract, the esophagus and the bronchi: a fluorescence microscopy study", *J. Photochem. Photobiol. B: biol.*, 61, pp 1-9, 2001.

57) N. Lange, J.-P. Ballini, G. Wagnières and H. van den Bergh, "A new Drug-Screening Procedure for Photosensitizing Agents used in Photodynamic Therapy of Choroidal Neovascularization", *Investigative Ophthalmology & Visual Science*, 42(1), pp 38-46, 2001.

56) M. Zellweger, P. Grosjean, D. Goujon, Ph. Monnier, H. van den Bergh and G. Wagnières, "Autofluorescence spectroscopy to characterize the histopathological status of bronchial tissue in vivo", *J. of Biomedical Optics*, 6(1), pp 41-52, 2001.

55) M. Zellweger, D. Goujon, M. Forrer, H. van den Bergh and G. Wagnières, "Absolute autofluorescence spectra of healthy bronchial tissue in vivo", *Applied Optics*, 40(22), pp 3784-3791, 2001.

54) Th. Glanzmann, M. Forrer, S. Andrejevic Blant, A. Woodtli, P. Grosjean, D. Braichotte, H. van den Bergh, Ph. Monnier and G. Wagnières, "Pharmacokinetics and Pharmacodynamics of tetra(m-hydroxyphenyl)chlorin in the Hamster Cheek Pouch Tumor Model: Comparison with Clinical Measurements", *J. Photochem. Photobiol. B: Biol.*, 57, pp 22-32, 2000.

53) S. Andrejevic Blant, J.-P. Ballini, H. van den Bergh, Ch. Fontolliet, G. Wagnières and Ph. Monnier, "Time dependent biodistribution of tetra(m-hydroxyphenyl)chlorin and benzoporphyrin derivative monoacid ring A in the hamster model: comparative fluorescence microscopy study", *Photochem. Photobiol.*, 71(3), pp 333-340, 2000.

52) M. Zellweger, A. Radu, Ph. Monnier, H. van den Bergh and G. Wagnières, "In vivo pharmacokinetics of Lutetium Texaphyrin in the healthy and tumoral cheek pouch mucosa. Retention and selectivity properties", *J. Photochem. Photobiol. B: Biol.*, 55(1), pp 56-62, 2000.

51) A. Radu, G. Wagnières, H. van den Bergh, and Ph. Monnier, "Photodynamic therapy of early squamous cell cancers of the esophagus", *Gastrointestinal endoscopy Clin North America*, 10(3), pp 439-460, 2000.

50) R. Bays, A. Woodtli, L. Mosimann, P. Wyss, G. Wagnières, U. Haller, H. van den Bergh, "A light distributor for photodynamic endometrial ablation", *Photomedicine in Gynecology and Reproduction*; P. Wyss, Y. Tadir, B. Tromberg, U. Haller: Authors Editors, Karger, Basel, pp 227-233, 2000.

49) P. Uehlinger, M. Zellweger, G. Wagnières, L. Juillerat, H. van den Bergh and N. Lange, "5-Aminolevulinic acid and its derivatives: physical chemical properties and protoporphyrin IX formation in cultured cells", *J. Photochem. Photobiol. B: Biol.*, 54, pp 72-80, 2000.

48) S. Iinuma, K. T. Schomacker, G. Wagnières, M. Rajadhyaksha, M. Bamberg, T. Momma and T. Hasan, "In vivo fluence rate and fractionation effects on tumor response and photobleaching: photodynamic therapy with two photosensitizers in an orthotopic rat tumor model", *Cancer Res (United States)*, 59(24), pp 6164-6170, 1999.

47) J. Mizeret, Th. Stepinac, M. Hansroul, A. Studzinski, H. van den Bergh and G. Wagnières, "Instrument for real-time endoscopic fluorescence lifetime imaging", *Rev. Sci. Instrum.*, 70(12), pp 4689-4701, 1999.

46) Th. Glanzmann, J.-P. Ballini, H. van den Bergh and G. Wagnières, "Time-resolved spectrofluorometer for clinical tissue characterization", *Rev. Sci. Instrum.*, 70(10), pp 4067-4077, 1999.

45) M. Zellweger, P. Grosjean, Ph. Monnier, H. van den Bergh and G. Wagnières, "Stability of the fluorescence measurement of Foscan® in the normal human oral cavity as an indicator of its content in early cancers of the esophagus and the bronchi", *Photochem. Photobiol.*, 69(5), pp 605-610, 1999.

44) N. Lange, P. Jichlinski, M. Zellweger, M. Forrer, A. Marti, L. Guillou, P. Kucera, G. Wagnières and H. van den Bergh, "Photodetection of early human bladder cancer based on the fluorescence of 5-aminolevulinic acid hexylester-induced protoporphyrin IX: a pilot study", *Brit. J. Cancer*, 80(1/2), pp 185-193, 1999.

43) A. Radu, P. Grosjean, Ch. Fontolliet, G. Wagnières, A. Woodtli, H. van den Bergh and Ph. Monnier, "Photodynamic Therapy for 101 Early Cancers of the Upper Aerodigestive Tract, the Esophagus, and the Bronchi: A single-Institution Experience", *Diagnostic and Therapeutic Endoscopy*, 5, pp 145-154, 1999.

42) G. Wagnières, W. Star and B. Wilson, "In vivo fluorescence spectroscopy and imaging for oncological applications", *Photochem. Photobiol.*, 68(5), pp 603-632, 1998.

41) G. Wagnières, Ch. Hadjur, P. Grosjean, D. Braichotte, J.-F. Savary, Ph. Monnier and H. van den Bergh, "Clinical evaluation of the cutaneous phototoxicity of 5, 10, 15, 20-tetra(m-hydroxyphenyl)chlorin", *Photochem. Photobiol.*, 68(3), pp 382-387, 1998.

40) Ch. Hadjur, N. Lange, J. Rebstein, Ph. Monnier, H. van den Bergh and G. Wagnières "Spectroscopic studies of photobleaching and photoproduct formation of meta(tetrahydroxyphenyl)chlorin (mTHPC) used in photodynamic therapy. The production of singlet oxygen by mTHPC", *J. Photochem. Photobiol. B: Biology*, 45, pp 170-178, 1998.

39) A. Kienle, Th. Glanzmann, G. Wagnières, H. van den Bergh, "Investigation of two-layered turbid media with time-resolved reflectance", *Applied Optics*, 37(28), pp 6852-6862, 1998.

38) Th. Glanzmann, Ch. Hadjur, M. Zellweger, P. Grosjean, M. Forrer, J.-P. Ballini, Ph. Monnier, H. van den Bergh, Ch. Lim and G. Wagnières, "Pharmacokinetics of Tetra(m-hydroxyphenyl)chlorin in Human Plasma and Individualized Light Dosimetry in Photodynamic Therapy", *Photochem. Photobiol.*, 67(5), pp 596-602, 1998.

37) N. Dögnitz and G. Wagnières, "Determination of Tissue Optical Properties by Steady State Spatial Frequency-domain Reflectometry", *Lasers in Med. Sci.*, 13, pp 55-65, 1998.

36) P. Grosjean, G. Wagnières, Ch. Fontolliet, H. van den Bergh and Ph. Monnier, "Clinical photodynamic therapy with Photofrin II and 514 nm light for superficial cancers in the oesophagus and the bronchi", *Brit. J. of Cancer*, 77(11), pp 1989-1995, 1998.

35) P. Westermann, Th. Glanzmann, S. Andrejevic, D. Braichotte, M. Forrer, G. Wagnières, Ph. Monnier, H. van den Bergh, J.-P. Mach and S. Folli, "Long circulating half-life and high tumor selectivity of the photosensitizer meta-tetrahydroxyphenylchlorin conjugated to polyethylene-glycol in nude-mice grafted with a human colon-carcinoma" *Int. J. Cancer*, 76(6), pp 842-850, 1998.

34) S. Andrejevic-Blant, A. Woodtli, G. Wagnières, Ch. Fontolliet, H. van den Bergh and Ph. Monnier, "Interstitial photodynamic therapy with tetra(m-hydroxyphenyl)chlorin: tumor versus striated muscle damage", *Int. J. of Radiation Oncology Biol. Phys.*, 42(2), pp 403-412, 1998.

33) J.-F. Savary, P. Grosjean, Ph. Monnier, Ch. Fontolliet, G. Wagnières, D. Braichotte and H. van den Bergh, "Photodynamic therapy of early squamous cell carcinomas of the eosophagus: a review of 31 cases", *Endoscopy*, 30, pp 258-265, 1998.

32) A. Kienle, M. Patterson, N. Dögnitz, R. Bays, G. Wagnières and H. van den Bergh, "Noninvasive determination of the optical properties of two-layered turbid media", *Applied Optics*, 37(4), pp 779-791, 1998.

31) G. Wagnières, J. Mizeret, A. Studzinski and H. van den Bergh, "Frequency-Domain Fluorescence Lifetime Imaging for Endoscopic Clinical Cancer Photodetection: Apparatus Design and Preliminary Results", *J. of Fluorescence*, 7(1), pp 75-83, 1997.

30) G. Wagnières, A. Studzinski and H. van den Bergh, "An endoscopic fluorescence imaging system for simultaneous visual examination and photodetection of cancers", *Rev. Sci. Instrum.*, 68, pp 203-212, 1997.

29) S. Andrejevic Blant, Ch. Hadjur, J.-P. Ballini, G. Wagnières, Ch. Fontolliet, H. van den Bergh and Ph. Monnier, "Photodynamic therapy of early squamous cell carcinoma with tetra(m-hydroxyphenyl)chlorin: Optimal drug-light interval", *Brit. J. of Cancer*, 76(8), pp 1021-1028, 1997.

28) G. Wagnières, S. Cheng, M. Zellweger, N. Utke, D. Braichotte, J.-P. Ballini and H. van den Bergh, "An optical phantom with tissue-like properties in the visible for use in PDT and fluorescence spectroscopy", *Phys. Med. Biol.*, 42, pp 1-12, 1997.

27) P. Jichlinski, G. Wagnières, M. Forrer, J. Mizeret, L. Guillou, F. Schmidlin, P. Graber, H. van den Bergh et H.-J. Leisinger, "Intérêt clinique de la cystoscopie à fluorescence dans la détection des carcinomes à épithélium de transition superficiels de la vessie", *Annales d'Urologie*, 31(1), pp 43-48, 1997.

26) J. Mizeret, G. Wagnières, Th. Stepinac and H. van den Bergh, "Endoscopic Tissue Characterization by Frequency-Domain Fluorescence Lifetime Imaging", *Lasers in Medical Science*, 12(3), pp 209-217, 1997.

25) S. Andrejevic Blant, J.-F. Theumann, M. Forrer, G. Wagnières, H. van den Bergh and Ph. Monnier, "Wavelength-dependent effect of tetra(m-hydroxyphenyl)chlorin for photodynamic therapy in an "early" squamous cell carcinoma model", *Lasers in Medical Science*, 12(3), pp 269-273, 1997.

24) Ch. Hadjur, G. Wagnières, F. Ihringer, Ph. Monnier and H. van den Bergh, "Production of free Radicals O_2^- and OH by Irradiation of the Photosensitizer Zinc(II) Phthalocyanine", *Journal of Photochem. Photobiol. B: Biology*, 38, pp 196-202, 1997.

23) P. Jichlinski, G. Wagnières, M. Forrer, J. Mizeret, L. Guillou, M. Oswald, F. Schmidlin, P. Graber, H. van den Bergh et H.-J. Leisinger, "Clinical assessment of fluorescence cystoscopy during transurethral bladder resection in superficial bladder cancer", *Urological Research*, 25, pp S3-S6, 1997.

22) Ch. Hadjur, G. Wagnières, Ph. Monnier and H. van den Bergh, "EPR and Spectrophotometric studies of free Radicals (O_2^- , OH, BPD-MA $^-$) and Singlet Oxygen (1O_2) generated by Irradiation of Benzoporphyrin derivative Monoacid Ring A", *Photochem. Photobiol.*, 65(5), pp 818-827, 1997.

21) J. Inderfurth and G. Wagnières, "Photoinduction of Fluorophores in the Retina using a 514 nm Argon Ion Laser", *German Journal of Ophthalmology*, 6, pp 1-5, 1997.

20) R. Bays, G. Wagnières, D. Robert, J.-F. Theumann, A. Vitkin, J.-F. Savary, Ph. Monnier and H. van den Bergh, "Three-Dimensional Optical Phantom and its Application in Photodynamic Therapy", *Lasers in Surgery and Medicine*, 21(3), pp 227 - 234, 1997.

19) G. Wagnières, A. Studzinsky, D. Braichotte, Ph. Monnier, Ch. Depeursinge, A. Châtelain and H. van den Bergh, "Clinical imaging fluorescence apparatus for the endoscopic photodetection of early cancers using Photofrin II", *Applied Optics*, 36(13), pp 5608-5620, 1997.

18) J.-F. Savary, Ph. Monnier, Ch. Fontolliet, J. Mizeret, G. Wagnières, D. Braichotte and H. van den Bergh, "Photodynamic therapy for early squamous cell carcinomas of the eosophagus, bronchi and mouth with m-Tetra(Hydroxyphenyl) Chlorin", *Archives of Otolaryngol. Head Neck Surg.*, 123, pp 162-168, 1997.

17) R. Bays, G. Wagnières, D. Robert, D. Braichotte, J.-F. Savary, Ph. Monnier and H. van den Bergh, "Light dosimetry for photodynamic therapy in the Esophagus", *Lasers in Surgery and Medicine*, 20(3), pp 290-303, 1997.

16) P. Jichlinski, M. Forrer, J. Mizeret, Th. Glanzmann, D. Braichotte, G. Wagnières, G. Zimmer, L. Guilloud, F. Schmidlin, P. Graber, H. van den Bergh and H.-J. Leisinger, "Clinical evaluation of a method for detecting superficial transitional cell carcinoma of the bladder by light induced fluorescence of Protoporphyrin IX following topical application of 5-aminolevulinic acid: Preliminary results", *Lasers in Surgery and Medicine*, 20(4), pp 402-408, 1997.

15) F. Schmidlin, P. Jichlinski, G. Delacrétaz, G. Wagnières, H.-J. Leisinger et P. Graber, "Les indications et performances du laser en urologie", Médecine et Hygiène, 54, pp 2208 - 2213, 1996.

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Oral presentations

Presentations given by G. Wagnières as invited speaker at international conferences (with financial support):

- "Instrumentation developped for the cancer photodynamic therapy in the upper aero-digestive tract", Meeting on PDT and Photodiagnosis: present state and future aspects, Meeting Hoffmann La Roche, Basel, July 1987.
- "Tissue characterization using environmentally sensitive fluorochromes", OE/LASE '94, Biomedical Optics, Los Angeles, USA, January 1994.

- "Measurement of the Photofrin II absolute fluorescence quantum yield in Tissue", 22nd Annual Meeting of the American Society for Photobiology, Scottsdale, Arizona, U.S.A., June 1994.
- "Les diffuseurs de lumière", Actualités en Thérapie Photodynamique, Paris, France, December 1996.
- "Clinical and Preclinical Measurements of fluorescence and photobleaching to optimize PDT and understand its kinetics", OE/LASE '97, International Biomedical Optics Symposium, San Jose, California, USA, February 1997.
- "Measurement of the benzoporphyrin derivative (BPD-MA) absolute fluorescence quantum yield in tissue", BiOS Europe '97, San Remo, Italy; September 1997.
- "Fluorescence lifetime imaging for endoscopic tissue characterization", 13th International Congress on Photobiology, Stresa, Italy, September 1997.
- "Clinical evaluation of the cutaneous phototoxicity of a second generation photosensitizer for PDT: mTHPC", PDT Physics Association Meeting, Scotia House, Stirling, Scotland, December 1997.
- "Laser tissue interaction: Photochemical effects", International Symposium on lasers in urology, Zürich, Switzerland; 4-6 March 1999.
- "Study of the tissue autofluorescence spectroscopy to optimize the detection of human bronchial precancerous and early cancerous lesions", Photodiagnosis and Photodynamic therapy in Clinical Practice, Innsbruck, Austria, 21-23 October 1999.
- "Tissue Fluorescence Spectroscopy", 7th United European Gastroenterology Week, Roma, Italy; 13-17 November 1999.
- "Basic principles of Photodynamic Therapy", 9th Congress of the European Academy of Dermatology & Venereology, Geneva, Switzerland; 11-15 October 2000.
- "Endoscopic tissue fluorescence spectroscopy to optimize the imaging photodetection of precancerous and early cancerous lesions", Photonics West, San Jose, USA; 19-25 January 2002.
- "Spectral Fluorescence Endoscopy", 12th World Congress for Bronchology, Boston, MA, USA; 16-19 June 2002.
- "La thérapie photodynamique: Principe, aspects instrumentaux et monitorage de la dose thérapeutique", XXIIIème Congrès de la SFLM, Arcs 1800, France; 26-29 January 2003.
- "First experience of hexyl-ester aminolevulinic acid induced fluorescence cystoscopy in patients with superficial bladder cancer", European Conference on Biomedical Optics, Munich, Germany; 22-25 June, 2003.
- "Detection of precancerous and early cancerous lesions in the bronchi by fluorescence/reflectance imaging with a spectrally optimized system", 10th Conference of the European Society for Photobiology, Vienna, Austria; 6-11 September, 2003.

Other oral presentations given by G. Wagnières at international conferences:

- "Instrumental aspects of light delivery for PDT in the upper aerodigestive tract", 2nd International Conference on Photodynamic Therapy and Medical Laser Applications, London, England, July 1988.
- "Detection of "Early" cancer in the upper aerodigestive tract and bronchi by fluorescence endoscopy: Apparatus and clinical results", 3rd International Conference on Photodynamic Therapy, Buffalo, USA, July 1990.
- "Measurement of the Photofrin II absolute fluorescence quantum yield in tissue", 4th International Conference on Photodynamic Therapy, Milan, Italy, June 1992.
- "Clinical evaluation of the photodamage to tumors, normal tissue and skin in PDT with mTHPC and Photofrin II", SPIE's international Symposium on Laser Engineering, Optoelectronic Packaging and Interconnects and Biomedical Optics, Los Angeles, U.S.A., January 1993.
- "Clinical measurements of tissue optical properties in the esophagus", BiOS Europe '94, International Symposium on Biomedical Optics, Lille, France, September 1994.
- "Clinical Measurement of Tissue Optical Properties in the Esophagus and in the Oral Cavity", 5th International Photodynamic Association Biennial Meeting, Amelia Island, Florida, USA, September 1994.
- "Caractérisation endoscopique de lésions cancéreuses précoces par spectrofluorométrie de fluorophores exogènes: applications cliniques", OPT-DIAG '95: Diagnostic et imagerie optiques en médecine, Paris, France, Mai 1995.
- "Measurement of the m-THPC absolute fluorescence quantum yield in tissue", European Biomedical Optics, BiOS Europe '95, Barcelona, Spain, September 1995.
- "Clinical Optimization in Photodynamic Therapy of early Squamous Cell Carcinoma located in the esophagus and the Tracheo-bronchial tree by endoscopic fluorescence spectroscopy", 6th Biennial Meeting of the International Photodynamic Association, Melbourne, Australia, March 1996.
- "Design and characterization of a phantom simulating the tissue optical properties over the visible part of the spectrum", BiOS Europe '96, Vienna, Austria, September 1996.
- "Clinical evaluation of the cutaneous phototoxicity of mTHPC", Seventh Biennial Congress of the International Photodynamic Association, Nantes, France; 7-9 July, 1998.
- "Clinical study of the mTHPC-induced tissue photosensitization under various conditions", BiOS Europe '98: Norra Latin Conference Center Stockholm, Sweden; 8-12 September 1998.
- "Frequency-domain fluorescence lifetime imaging (FLIM) for real-time endoscopy tissue characterization" CLEO/Europe, Münich, Germany; 13-16 June 1999.
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- "Détection de dysplasies et de cancers précoce dans l'oesophage de Barrett par imagerie endoscopique de fluorescence de la protoporphyrine IX après administration orale d'acide delta-aminolévulinique", OPT-DIAG 2002: Diagnostic et imagerie optiques en médecine, Paris, France, Mai 2002.

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U.S. Patent: 5,054,867
European Patent: 0437181
Inventors: G. Wagnières, H. van den Bergh, Ph. Monnier
- 3) Apparatus for homogenising the non-homogeneous light distribution of a laser beam.
U.S. Patent: 5,068,515
European Patent: 0435825
Inventors: H. van den Bergh, P. Cornaz, G. Wagnières
- 4) Device for injecting the light energy of a laser beam into a fibre-optical waveguide and a method for adjusting and monitoring the position of the end of the fibre-optic optical waveguide.
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- 5) Fibre-optic apparatus for the photodynamic treatment of tumours.
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Inventors: G. Wagnières, H. van den Bergh, Ph. Monnier
- 6) Light diffuser for the photodynamic therapy of tumours in the oesophagus of a patient.
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European Patent: 0437183
Inventors: G. Wagnières, H. van den Bergh, Ph. Monnier
- 7) Device for irradiating internal cavities of the body

WO9911322

Inventors: R. Bays, A. Woodtli, G. Wagnières, H. van den Bergh

8) Diagnosis apparatus for the picture providing recording of fluorescing biological tissue regions.
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Inventors: G. Wagnières, M. Zellweger, N. Chauvin, N. Lange, U. Zanger, A. Studzinski, H. van den Bergh

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